

=> s astemizole/cn  
L1 1 ASTEMIZOLE/CN

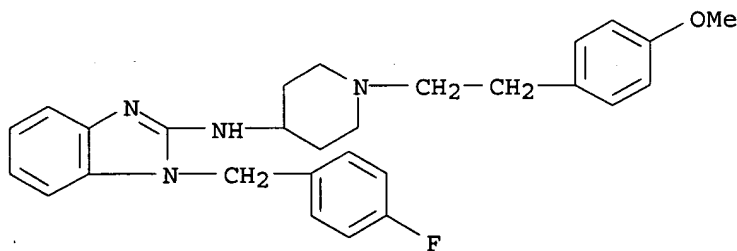
=> d

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN  
RN 68844-77-9 REGISTRY  
ED Entered STN: 16 Nov 1984  
CN 1H-Benzimidazol-2-amine, 1-[(4-fluorophenyl)methyl]-N-[1-[2-(4-methoxyphenyl)ethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN Astemisan  
CN Astemizole  
CN Hismanal  
CN Histamen  
CN Histaminos  
CN Histazol  
CN Kelp  
CN Laridal  
CN Metodik  
CN Novo-Nastizol A  
CN NSC 329963  
CN Paralergin  
CN R 42512  
CN R 43512  
CN Retolen  
CN Waruzol  
MF C28 H31 F N4 O  
CI COM

LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HSDB\*, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK\*, MSDS-OHS, PHAR, PROMT, PROUSDDR, PS, RTECS\*, SCISEARCH, SPECINFO, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU  
(\*File contains numerically searchable property data)  
Other Sources: EINECS\*\*, WHO  
(\*\*Enter CHEMLIST File for up-to-date regulatory information)



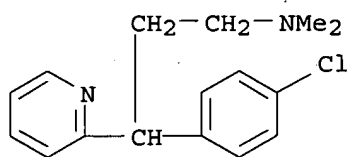
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

619 REFERENCES IN FILE CA (1907 TO DATE)  
17 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
622 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s chlorpheniramine/cn  
L2 1 CHLORPHENIRAMINE/CN

=> d

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN  
 RN 132-22-9 REGISTRY  
 ED Entered STN: 16 Nov 1984  
 CN 2-Pyridinepropanamine,  $\gamma$ -(4-chlorophenyl)-N,N-dimethyl- (9CI) (CA  
 INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN Pyridine, 2-[p-chloro- $\alpha$ -[2-(dimethylamino)ethyl]benzyl]- (8CI)  
 OTHER NAMES:  
 CN ( $\pm$ )-Chloropheniramine  
 CN ( $\pm$ )-Chloropheniramine  
 CN  $\gamma$ -(4-Chlorophenyl)- $\gamma$ -(2-pyridyl)propyldimethylamine  
 CN 1-(p-Chlorophenyl)-1-(2-pyridyl)-3-dimethylaminopropane  
 CN 2-[p-Chloro- $\alpha$ -[2-(dimethylamino)ethyl]benzyl]pyridine  
 CN 3-(p-Chlorophenyl)-3-(2-pyridyl)-N,N-dimethylpropylamine  
 CN 4-Chloropheniramine  
 CN Allergican  
 CN Chlorophenamine  
 CN Chloropheniramine  
 CN Chlorophenylpyridamine  
 CN Chloroprophenpyridamine  
 CN Chlorphenamine  
 CN Chlorpheniramine  
 CN Chloroprophenpyridamine  
 CN dl-1-(p-Chlorophenyl)-1-(2-pyridyl)-3-(dimethylamino)propane  
 CN Haynon  
 CN RS-Chloropheniramine  
 FS 3D CONCORD  
 DR 42882-96-2, 46970-45-0  
 MF C16 H19 Cl N2  
 CI COM  
 LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOSIS, BIOTECHNO,  
 CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN,  
 CSCHM, DDFU, DRUGU, EMBASE, HSDB\*, IFICDB, IFIPAT, IFIUD, IPA,  
 MEDLINE, MRCK\*, PHAR, PROMT, PS, RTECS\*, SPECINFO, TOXCENTER, USAN,  
 USPAT2, USPATFULL, VETU  
 (\*File contains numerically searchable property data)  
 Other Sources: EINECS\*\*, NDSL\*\*, TSCA\*\*, WHO  
 (\*\*Enter CHEMLIST File for up-to-date regulatory information)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

810 REFERENCES IN FILE CA (1907 TO DATE)  
 26 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 813 REFERENCES IN FILE CAPLUS (1907 TO DATE)  
 7 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

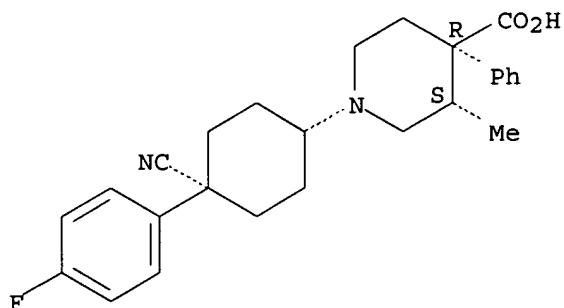
=> s levocabastine/cn  
 L3 1 LEVOCABASTINE/CN

=> d

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN  
 RN 79516-68-0 REGISTRY

ED Entered STN: 16 Nov 1984  
 CN 4-Piperidinecarboxylic acid, 1-[cis-4-cyano-4-(4-fluorophenyl)cyclohexyl]-3-methyl-4-phenyl-, (3S,4R)- (9CI) (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN 4-Piperidinecarboxylic acid, 1-[4-cyano-4-(4-fluorophenyl)cyclohexyl]-3-methyl-4-phenyl-, [3S-[1(cis),3 $\alpha$ ,4 $\beta$ ]]-  
 OTHER NAMES:  
 CN Levocabastine  
 CN Levophta  
 CN R 50547  
 FS STEREOSEARCH  
 MF C26 H29 F N2 O2  
 CI COM  
 LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN\*, BIOSIS, BIOTECHNO, CA, CAPLUS, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK\*, PHAR, PROMT, PROUSDDR, PS, SCISEARCH, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL  
 (\*File contains numerically searchable property data)  
 Other Sources: WHO

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

196 REFERENCES IN FILE CA (1907 TO DATE)  
 5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 196 REFERENCES IN FILE CAPLUS (1907 TO DATE)

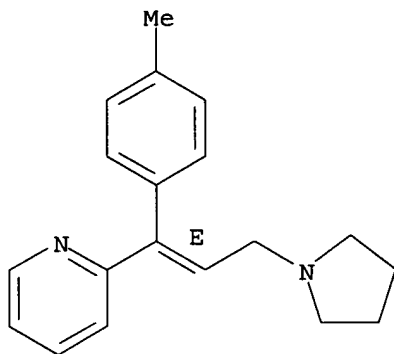
=> s triprolidine/cn  
 L4 1 TRIPROLIDINE/CN

=> d

L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN  
 RN 486-12-4 REGISTRY  
 ED Entered STN: 16 Nov 1984  
 CN Pyridine, 2-[(1E)-1-(4-methylphenyl)-3-(1-pyrrolidinyl)-1-propenyl]- (9CI)  
 (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN Pyridine, 2-[1-(4-methylphenyl)-3-(1-pyrrolidinyl)-1-propenyl]-, (E)-  
 CN Pyridine, 2-[3-(1-pyrrolidinyl)-1-p-tolylpropenyl]-, (E)- (8CI)  
 OTHER NAMES:  
 CN trans-1-(2-Pyridyl)-3-pyrrolidino-1-p-tolylprop-1-ene  
 CN trans-1-(4-Methylphenyl)-1-(2-pyridyl)-3-pyrrolidinoprop-1-ene  
 CN trans-2-[3-(1-Pyrrolidinyl)-1-p-tolylpropenyl]pyridine  
 CN Triprolidin  
 CN Triprolidine

CN Tripyrolidine  
 FS STEREOSEARCH  
 MF C19 H22 N2  
 CI COM  
 LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOSIS, BIOTECHNO,  
 CA, CAOLD, CAPLUS, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE,  
 HSDB\*, IFICDB, IFIUDb, IPA, MEDLINE, MRCK\*, PROMT, PS, RTECS\*, SPECINFO,  
 TOXCENTER, USAN, USPAT2, USPATFULL  
 (\*File contains numerically searchable property data)  
 Other Sources: EINECS\*\*, WHO  
 (\*\*Enter CHEMLIST File for up-to-date regulatory information)

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

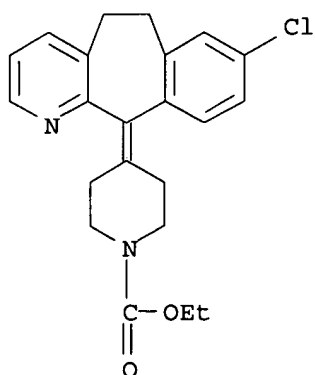
429 REFERENCES IN FILE CA (1907 TO DATE)  
 10 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 430 REFERENCES IN FILE CAPLUS (1907 TO DATE)  
 3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> s loratidine/cn  
 L5 1 LORATIDINE/CN

=> d

L5 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN  
 RN 79794-75-5 REGISTRY  
 ED Entered STN: 16 Nov 1984  
 CN 1-Piperidinecarboxylic acid, 4-(8-chloro-5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)-, ethyl ester (9CI) (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN 11H-Benzo[5,6]cyclohepta[1,2-b]pyridine, 1-piperidinecarboxylic acid deriv.  
 OTHER NAMES:  
 CN Alavert  
 CN Anhissen  
 CN Bonalerg  
 CN Civeran  
 CN Claratyne  
 CN Claritin  
 CN Claritine  
 CN Clarityn  
 CN Clarityne

CN Cronopen  
 CN Flonidan  
 CN Fristamin  
 CN Histaloran  
 CN Klaritin  
 CN Lertamine  
 CN Lisino  
 CN Loracert  
 CN Loradex  
 CN Loranox  
 CN Lorastine  
 CN Loratadine  
 CN Loratidine  
 CN Loratyne  
 CN Lorfast  
 CN Lowadina  
 CN Optimin  
 CN Polaratyne  
 CN Pylor  
 CN Restamine  
 CN Sch 29851  
 CN Sensibit  
 CN Sohotin  
 CN Tadine  
 CN Velodan  
 CN Zeos  
 MF C22 H23 Cl N2 O2  
 CI COM  
 LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOSIS,  
 BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHM, DDFU,  
 DRUGU, EMBASE, HSDB\*, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH,  
 IPA, MEDLINE, MRCK\*, PHAR, PIRA, PROMT, PROUSDDR, PS, RTECS\*, SCISEARCH,  
 SPECINFO, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU  
 (\*File contains numerically searchable property data)  
 Other Sources: WHO

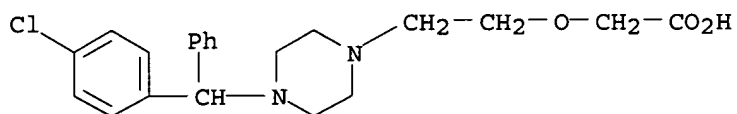


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

911 REFERENCES IN FILE CA (1907 TO DATE)  
 21 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 915 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s cetirizine/cn  
 L6 1 CETIRIZINE/CN  
 => d

L6 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN  
 RN 83881-51-0 REGISTRY  
 ED Entered STN: 16 Nov 1984  
 CN Acetic acid, [2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy] -  
 (9CI) (CA INDEX NAME)  
 OTHER NAMES:  
 CN (+)-Cetirizine  
 CN Cetirizine  
 FS 3D CONCORD  
 DR 130018-86-9  
 MF C21 H25 Cl N2 O3  
 CI COM  
 LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, BIOTECHNO,  
 CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE,  
 IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK\*,  
 PHAR, PROMT, PROUSDDR, PS, RTECS\*, SCISEARCH, SYNTHLINE, TOXCENTER,  
 USAN, USPAT2, USPATFULL, VETU  
 (\*File contains numerically searchable property data)  
 Other Sources: WHO



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

765 REFERENCES IN FILE CA (1907 TO DATE)  
 17 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 769 REFERENCES IN FILE CAPLUS (1907 TO DATE)

AN 2002:190182 CAPLUS  
TI Design and synthesis of novel dual histamine H1/H3 receptor antagonists  
based on the H1 receptor antagonist chlorpheniramine  
AU Aslanian, Robert; Mutahi, Mwangi W.; Tom, Wing; Shih, Neng-Yang; Piwinski,  
John J.; West, Robert; Williams, Shirley M.; She, Susan  
CS Department of Chemical Research, Schering Plough Research Institute,  
Kenilworth, NJ, 07033, USA  
SO Abstracts of Papers, 223rd ACS National Meeting, Orlando, FL, United  
States, April 7-11, 2002 (2002), MEDI-063 Publisher: American Chemical  
Society, Washington, D. C.  
CODEN: 69CKQP  
DT Conference; Meeting Abstract  
LA English  
TI Design and synthesis of novel dual histamine H1/H3 receptor antagonists  
based on the H1 receptor antagonist chlorpheniramine  
AB Allergic rhinitis is a disease characterized by sneezing, rhinorrhea,  
pruritus, and nasal congestion. H1 antihistamines are effective  
at treating the first three symptoms, but are ineffective at treating  
nasal congestion. To improve their therapeutic profile, H1  
antihistamines have been combined with  $\alpha$ -agonist decongestants such  
as pseudoephedrine or phenylpropanolamine. However,  $\alpha$ -agonists are  
contraindicated in individuals with cardiovascular or prostatic disease.  
Therefore, new methods for treating nasal congestion are desirable.  
Recent work has demonstrated that concurrent administration of a  
selective H1 antagonist with a selective  
H3 antagonist is decongesting in a histamine-driven cat model of  
nasal congestion. In light of this data, we set out to determine if a single  
chemical entity could be designed that would inhibit both the  
H1 and H3 receptors simultaneously. This paper will  
describe the discovery of novel dual antagonists of the histamine  
H1 and H3 receptors based on the selective  
H1 antagonist chlorpheniramine.

12167505 PMID: 10582118

Combined histamine H1 and H3 receptor blockade produces nasal decongestion in an experimental model of nasal congestion.

McLeod R L; Mingo G G; Herczku C; DeGennaro-Culver F; Kreutner W; Egan R W; Hey J A

Allergy Department, Schering-Plough Research Institute, Kenilworth, NJ 07033-0539, USA.

American journal of rhinology (UNITED STATES) Sep-Oct 1999, 13 (5) p391-9, ISSN 1050-6586--Print Journal Code: 8807268

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS; Toxbib

We studied the pharmacological actions of combined histamine H1/H3 receptor blockade on the increase in nasal airway resistance (NAR) and decrease in nasal cavity volume produced by nasal exposure to compound 48/80, a mast cell degranulator. In the anesthetized cat compound 48/80 (1%) produced a maximum increase in NAR of  $9.1 \pm 0.7$  cmH<sub>2</sub>O/L/minute. The increase in NAR in animals pretreated with a \*\*\*combination\*\*\* of the H1 antagonist, chlorpheniramine (CTM; 0.8 mg/kg i.v.) and increasing doses of the H3 antagonist, thioperamide (THIO; 1.0, 3.0, and 10.0 mg/kg i.v.) were  $6.1 \pm 2.1$ ,  $4.2 \pm 1.0$  and  $2.2 \pm 0.7$  cmH<sub>2</sub>O/L/minute, respectively. A second H3 antagonist, clobenpropit (CLOB; 0.03, 0.3, and 1.0 mg/kg i.v.) \*\*\*combined\*\*\* with CTM (0.8 mg/kg i.v.) also inhibited the nasal effects of compound 48/80. When the non-sedating H1 antihistamine, loratadine (3.0 mg/kg i.v.), was substituted for CTM, it also reduced nasal congestion when given in combination with THIO (10 mg/kg i.v.). In contrast, treatment with CTM (1.0 mg/kg i.v.) and the H2 antagonist, ranitidine (RAN; 1.0 mg/kg i.v.) were without activity. Loratadine, CTM, CLOB, RAN, or THIO administered alone were inactive. The alpha-adrenergic agonist, phenylpropanolamine (PPA; 1.0 mg/kg i.v.) demonstrated decongestant effects, but in contrast to H1/H3 blockade, PPA produced a significant hypertensive effect. Using acoustic rhinometry (AcR) we found that \*\*\*combined\*\*\* i.v. CTM (1.0 mg/kg) and THIO (10 mg/kg) and combined oral CTM (10 mg/kg) and THIO (30 mg/kg) blocked the decrease in nasal cavity volume produced by intranasal compound 48/80 (1%, 50 microL). We conclude that \*\*\*combined\*\*\* \*\*\*H1\*\*\* / \*\*\*H3\*\*\*

histamine receptor blockade enhances the efficacy of an H1 antagonist by conferring decongestant activity to the H1 antihistamine. We propose that the decongestant activity of combined H1/H3 blockade may provide a novel approach for the treatment of allergic nasal congestion without the hypertensive liability of current therapies.

Tags: Male

Descriptors: \*Chlorpheniramine--therapeutic use--TU; \*Disease Models, Animal; \*Histamine Antagonists--therapeutic use--TU; \*Histamine H1 Antagonists--therapeutic use--TU; \*Nasal Decongestants--therapeutic use--TU; \*Nasal Obstruction--drug therapy--DT; \*Piperidines--therapeutic use--TU; Airway Resistance--drug effects--DE; Animals; Cats; Drug Evaluation, Preclinical; Drug Therapy, Combination; Histamine Release --drug effects--DE; Nasal Cavity--drug effects--DE; Nasal Cavity--pathology--PA; Nasal Obstruction--chemically induced--CI; Nasal Obstruction --physiopathology--PP; Nose--drug effects--DE; Nose--physiopathology--PP; p-Methoxy-N-methylphenethylamine

CAS Registry Number: 0 (Histamine Antagonists); 0 (Histamine H1 Antagonists); 0 (Nasal Decongestants); 0 (Piperidines); 106243-16-7 (thioperamide); 132-22-9 (Chlorpheniramine); 4091-50-3 (p-Methoxy-N-methylphenethylamine)

Record Date Created: 19991223

Record Date Completed: 19991223



13830654 PMID: 12113214

Histamine in health and disease.

Repka-Ramirez M Susana; Baraniuk James N

Georgetown University, Washington, DC, USA.

Clinical allergy and immunology (United States) 2002, 17 p1-25,

ISSN 1075-7910--Print Journal Code: 9431211

Contract/Grant No.: AI42403; AI; NIAID

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Histamine is a potent vasoactive agent, bronchial smooth muscle constrictor, and stimulant of nociceptive itch nerves. Activation of H1-receptors plays a central role in the immediate allergic reaction, but has less of an impact in chronic allergic disorders where inflammatory infiltrates, additional mediators such as LTC4/D4/E4 and cytokines, and structural remodeling occur. Histamine, through its H1-receptor-mediated activities, appears to be primarily a proinflammatory agent, yet it does have some homeostatic functions in gastric acid production (H2-receptors) and the central nervous system (predominantly H3-receptors) (97, 98). The realization that first-generation antihistamines often had mixed pharmacological properties (e.g., anticholinergic actions) and crossed the blood-brain barrier led to the development of the second-generation drugs, which are more selective for H1-receptors, have less access to the central nervous system, and, therefore, a more favorable benefit-to-risk ratio (therapeutic index). The potential for combined H1-H3-antagonists remains to be fully explored, but offers another exciting opportunity for this ever-expanding family of beneficial drugs. (98 Refs.)

Descriptors: \*Histamine--physiology--PH; Animals; Asthma--etiology --ET; Common Cold--etiology--ET; Endothelium, Vascular--cytology--CY; Histamine Release; Humans; Hypersensitivity--etiology--ET; Immunoglobulin E --immunology--IM; Research Support, U.S. Gov't, Non-P.H.S.; Research Support, U.S. Gov't, P.H.S.; Rhinitis, \*\*\*Allergic\*\*\*, Seasonal--etiology --ET; Urticaria--etiology--ET

CAS Registry No.: 37341-29-0 (Immunoglobulin E); 51-45-6 (Histamine)

Record Date Created: 20020712

Record Date Completed: 20020731